

### **REMARKS/ARGUMENTS**

Reconsideration of this application is requested. Claims 37-43, 45 and 46 remain active in the application subsequent to entry of this Amendment.

In the above Amendment claim 45 has been identified as being "New" claim responsive to the objection made on page 2 of the Official Action.

In addition, claim 44 has been rewritten in independent format, as discussed below.

Applicants now address the various issues raised in the outstanding Official Action in the order presented.

#### **Claims 39, 42-43 and 45 – 35 USC § 112**

The meaning of the term "a previous preparation reaction" will be understood from the context of the description of the invention, see page 14, line 13, where the advantage of re-use of reactants is described and, in particular, page 15, first paragraph. Therefore, the skilled reader will have no difficulty in understanding the meaning of the above term in the light of the disclosure.

#### **Claims 37-43 and 45 – 35 USC § 103**

As claim 44 is not objected or rejected, counsel understands it is patentable. Claim 44 is combined with claim 37 and is presented above as new claim 46.

Claims 37-43 and 45 are rejected as being unpatentable over the Frick et al article. Applicants respond to the various points in the rejection.

The Examiner's observation about the *in situ* formation of NaCl in the reaction disclosed by Frick et al. is correct.

But the observation about the formation of NaCl in the claimed process is not correct.

The simplest way to understand the claimed reaction is to look at Example 1 on page 21 of the description. The skilled reader will appreciate that sodium chloride is present in the reaction mixture as starting material and in certain, well defined proportions with the starting compound aspartic acid, as stated in the claim. Therefore, the presence of sodium chloride as one of the starting materials, and not its mere, stoichiometric formation from the reaction between sodium nitrite and hydrochloric acid, as stated by the Examiner, is totally undisclosed or even suggested by Frick et al's article.

The accurate calculation made by the Examiner does not show that bromosuccinic acid, the only enabling disclosure by Frick et al., is equivalent to chlorosuccinic acid and that the reaction conditions can be freely translated one into the other.

This consideration directly leads to the third argument made by the Examiner. There is no guidance in Frick et al. that moving from bromosuccinic acid to chlorosuccinic acid, the isolation step can be obviously changed from an extraction with organic solvent to a precipitation in water.

To be tenable an obviousness rejection must be based on factual elements found in the cited references and that a guidance on how to combine these factual elements is provided to skilled person, also giving a reasonable expectation of success and the provision of the expected result.

In the description of their invention (see page 13, line 11 to page 14, line 7) applicants discuss the cited Frick et al. reference, as already stated in the previous response.

The cited reference states, but not demonstrates, that chlorosuccinic acid yield is 70%; see page 621, diagram. The claimed process yields 80-81% (Example 1) and 86-87% (Example 2), with overall yield of 83-84% (see pages 22-23).

The only working example provided by Frick et al. provides bromosuccinic acid (an ultimately different compound) with a yield of 88%, but e.e. = 94%. This latter aspect is very important in stereoselective synthesis such as the one of the present invention, where the final product, S-(-)-chlorosuccinic acid is used for the stereochemical synthesis of L-(-)-carnitine, whose optical purity is of dramatic importance for its use as a drug (R-(+)-carnitine is toxic).

According to Frick et al.'s method, also a substantial amount of 5% of aspartic acid is present in the final reaction mixture (see the discussion in the application, page 14, first line).

If we now look at the Examples of the present invention, in Example 1, S-(-)-chlorosuccinic acid is obtained with a yield of 80-81%, but a comparison of impurities is in favor of the claimed invention (aspartic acid up to 0.2%). See also Example 2.

Therefore, the different reaction conditions of the claimed subject matter are not even suggested by Frick et al -- in particular, there is no suggestion on how to obtain better yields and higher purity.

MELLONI et al  
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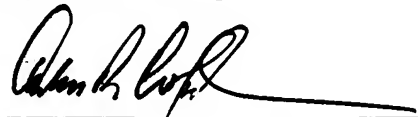
The Examiner's statement that extraction and precipitation can be used in isolation step is not predictive of better, unexpected results.

For the above reasons it is respectfully submitted that the claims of this application define inventive subject matter. Reconsideration of this application, entry of this Amendment and allowance are solicited. Should the examiner require further information or wish to discuss this application please contact the undersigned by telephone.

Respectfully submitted,

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